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Stimuli-triggered structural engineering of synthetic and biological polymeric assemblies

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ABSTRACT

Response to external stimuli is a fundamental and intrinsic behavior of living systems. There has been increasing interest for designing and constructing responsive polymeric superstructures by self-assembly. Stimuli-induced self-assembly and post-assembly triggering strategies provide an alternative approach for the manipulation of self-assembled architectures of either biological or synthetic polymeric materials. Stimuli-induced structural transformations may produce ensembles with new topologies or materials with exceptionally complex features inaccessible via conventional self-assembly processes. This is in contrast to materials that simply undergo stimuli-induced degradation, or disassembly processes. Since a variety of cellular processes depend on responses to environmental stimuli that lead to more complexity and increased function, and are related to structural transitions over the nano- to microscale, insights into stimuli-triggered morphogenesis can further deepen our understanding of cellular behaviors. Indeed, an understanding of these processes will likely inspire scientists to develop materials with advanced and tailored architectures for biosensing, diagnosis and therapy as well as other biomedical applications. Herein, we highlight state-of-the-art achievements in the stimuli-triggered structural manipulation of polymer assemblies. Furthermore, future developments in this nascent and growing field are briefly discussed.

Abbreviations: AFM, atomic force microscopy; ATP, adenosine triphosphate; CPB, polybutadiene with a terminal carboxyl group; 3D, three-dimensional; DAP, diamidopyridine; DETA, diethylenetriamine; DEX, dexamethasone; DIC, differential interference contrast; DLS, dynamic light scattering; DMF, dimethylformamide; DNA, deoxyribonucleic acid; DTT, dithiothreitol; EAB, ethyl 4-aminobenzoate; EDDA, 2,2′-(ethylenedioxy)diethylamine; EGTA, ethylene glycol tetraacetic acid; EtTrp, ethyl tryptophan; FCS, fluorescence correlation spectroscopy; IND, indomethacin; Ins(1,4,5)P_3, inositol 1,4,5-triphosphate; LCST, lower critical solution temperature; LCV, large compound vesicle; MAP, MT-associated protein; MNP, magnetic nanoparticle; MT, microtubule; NPC, nuclear pore complex; ODN, oligonucleotide; PAA, poly(acrylic acid); PAMAM, polyamidoamine; P*t*BA, poly(*tert*-butylacrylate); PBD, polybutadiene; PDI, polydispersity; PCEMA, poly(2-cinnamoyloxyethyl methacrylate); PCL, poly(ε-caprolactone); PEG, polyethylene glycol; PEI, polyethylenimine; PEO, poly(ethylene oxide); PI, polyisoprene; PIC, polyion complex; PIP_2, phosphatidylinositol-4,5-bisphosphate; PLL, polylysine; PLGA, poly(lactic-*co*-glycolic acid); PMA, poly(methyl acrylate); P2MVP, poly(*N*-methyl-2-vinyl pyridinium iodide); PNIPAAm, poly(*N*-isopropylacrylamide); PPO, poly(propylene oxide); PPS, poly(propylene sulfide); PS, polystyrene; PSGMA, poly(sucinnated glyceryl monomethacrylate); PSPP, poly(3-[*N*-(3-methacrylamido-propyl)-*N*,*N*-dimethyl]-ammonio propionate sulfonate); PTMC, poly(trimethylene carbonate); P4VP, poly(4-vinylpyridine); QD, quantum dot; SANS, small-angle neutron scattering; SAXRD, small-angle X-ray diffraction; SDS, sodium dodecyl sulfate; SEM, scanning electron microscopy; SFM, scanning force microscopy; SLS, static light scattering; TEM, transmission electron microscopy; TETA, triethylenetetraamine; Thy, thymine; UCST, upper critical solution temperature.

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Contents

1. Introduction

Response to external stimuli is a fundamental and intrinsic behavior of natural systems crucial for maintaining normal functions, performing advanced activities, and fighting diseases. For example, most of the immunological processes involve the antigen stimulation and subsequent cellular responses on the changed levels of cytokines and complements [1–3]. From unicellular organisms to advanced species, almost all the important biological processes are regulated by chemical, biological, or physical signals, including cell division, proliferation, differentiation, and apoptosis as well as respiration, photosynthesis and immunoregulation among them. More frequently, these responses are accompanied with structural transformation of self-organizing systems over various length scales from the molecular and cellular to the macroscopic [4,5]. At the molecular level, enzymes, ion channels and other transport proteins often undergo structural transitions that accommodate the binding of small molecules, ions or other substances. At a cellular level, biomembranes dynamically modulate their architectures by developing membrane curvature through interactions with a variety of molecules (Fig. 1), especially nanoscaled macromolecules such as synthetic polymers and proteins [6]. These conformational changes play important roles in cellular processes such as exocytosis, endocytosis, and vesicle budding (Fig. 1) [7]. For example, positive or negative membrane curvature can be generated upon inducing by amphipathic helix insertion, transmembrane or cytoskeletal proteins, thereby leading to a bilayer-to-vesicle transition (Fig. 2) [6].

Inspired by these biological systems, there is increasing interest in the development of supramolecular systems that can elaborately modulate their structures, and therefore obtain desirable characteristics and functions, in response to external stimuli like ions, molecules, temperature, and light [4,5,8–13]. Bottom–up self-assembly has been recognized as an efficient approach for fabricating highly functionalized molecular systems or even bio-entities [14]. Considerable effort has been directed toward assembling supramolecular structures via multiple-structured polymers during the past two decades [15–26]. Advances in this field have allowed the construction of supramolecular architectures with multiple morphologies across length scales. Polymer entities self-organized with various architectures or morphologies may have different performance characteristics with respect to disparate fields such as pharmaceuticals, biomedical engineering, optoelectronic devices and photovoltaics [27–31]. As has been demonstrated, modulation of the shape of polymer assemblies has most readily been implemented by tuning the molecular architecture of amphiphiles [19,32–35]. Nevertheless, morphology engineering through polymer structure always means the necessity of complicated or even time-consuming synthesis. As a consequence, manipulation of supramolecular assemblies with well-defined topology and size, without having to tailor the molecular structure of building blocks, is becoming one of the most important research focuses in the interdisciplinary field of supramolecular chemistry, polymer and material sciences, presenting a substantial scientific and engineering challenge. Recent studies